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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/597,592	06/16/2000	Heinrich Wieland	1378.001US1	4572

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EXAMINER	
HWU, JUNE	

ART UNIT	PAPER NUMBER
1661	

DATE MAILED: 03/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	09/597,592	WIELAND ET AL.	
	Examiner	Art Unit	
	June Hwu	1661	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed November 26, 2004 has been received. The foreign priority document filed December 30, 2004 has been received.

2. The Office action mailed on August 25, 2004 is being replaced with the following Office action. Any rejection not repeated herein is hereby withdrawn.

Status of the Claims

3. Claims 18-34 have been canceled. Claims 1-17 and 35 are examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-17, and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the determination of LDL triglyceride-containing lipoprotein wherein the A-B-A triblock copolymer of polyoxyethylene blocks A and central polyoxypropylene block B of molecular weight between 1000 and 8000 daltons and the molecular partial mass of polyoxypropylene block B is in the range of 75 to 95% by weight does not reasonably provide enablement for selective solubilization of triglyceride-containing lipoprotein with a nonionic surface active agent synthesized from a block copolymer of propylene oxide and ethylene oxide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

Breadth of the claims. The instant claims are drawn to a method of determining triglyceride (LDL, HDL, VLDL, CM, or IDL) contained in lipoprotein using a block copolymer of propylene oxide and ethylene oxide particularly the triblock copolymer A-B-A.

Nature of the invention. The claims are drawn to a selective solubilization of a triglyceride-containing lipoprotein with a non-ionic surface active agent, an A-B-A triblock copolymer of polyoxyethylene (POE) blocks A and central polyoxypropylene (POP) block B, the agent used for aggregating the lipoprotein is cyclodextrin or cyclodextrin derivative in the presence of divalent metal ions, and determining the triglyceride includes the enzymatic cleavage of the triglyceride with lipase or esterase.

Guidance in the specification. The specification provides little guidance regarding the method of determining triglyceride levels in HDL, VLDL, CM or IDL. On page 4, lines 26-28 and Example 1, the specification provides the molecular weight of POP/POE triblock copolymer in the range between 1000 and 8000 daltons and the molecular partial mass of POP/POE proportion range from 75-95% by weight for determining LDL triglycerides. Applicants have not specifically provided any information as to the molecular weight of the block copolymer for measuring triglycerides in HDL, VLDL, CM or IDL. Applicants also have not provided in the specification any copolymer combination within a particular molecular weight range that would be favorable for specific binding of the lipoprotein fractions. In addition, the specification does not disclose the molecular weight range of the POP/POE triblock copolymer for high-density lipoproteins (HDL), very low-density lipoproteins (VLDL), chylomicron (CM), or intermediate density lipoproteins (IDL).

Applicants state on page 3, lines 36-38, "The selectivity in relation to the individual lipoprotein fractions can be adjusted, as desired, by means of the composition of the POP/POE

block copolymer" but do not disclose in the specification what type of adjustment must be made for HDL, VLDL, CM and IDL determination.

Applicants further state in the specification on page 4, lines 34-39 and page 5, lines 3, that when the hydrophilic/lipophilic balance (HLB) is adjusted so that the LDL fraction is destabilized then the other lipoprotein fractions, HDL, VDL and CM, are stable. Hence, the triglycerides contained are unavailable or if available, in small quantity for the determination. Moreover, the selectivity in LDL is increased along with hydrophobicity in the molecular mass fraction of POP block B. Applicants have not provided any guidance in the specification as to the adjustment of the HBL so that the structure in the lipoprotein fraction (HDL, VLDL, CM or IDL) is destabilized while the other lipoprotein fractions remain stable.

Applicants have not described in the specification the particular conditions for the other lipoprotein fractions. Such condition for the claimed method would include the block copolymer formulation that would solubilize HDL, VLDL, CM or IDL lipoproteins. Although, the specification does demonstrate the triblock formulation, A-B-A, wherein the molecular weight of the formulation was 1000-8000 daltons and the molecular partial mass of polyoxypropylene block B is in the range of 75-95% by weight of the total triblock copolymer. The said guidance does not commensurate with the breadth being claimed since the composition of the block copolymer used would affect the selective solubilization of the particular triglyceride lipoprotein, namely, HDL, VLDL, CM or IDL. Without guidance as to the particular block copolymer formulations as described for specific binding of LDL, the skilled artisan would have to engage in undue trial and error experimentation to arrive at a particular formulation that would selectively solubilize any of the other triglycerides.

Existence of working examples. The working example in the specification describes the selective determination of LDL triglyceride. No other examples for the determining HDL, VDL, IDL and CM are disclosed.

Amount of experimentation necessary. It would require undue trial and error experimentation for one skilled in the art to determine the block units' combination and their ratio for determining the triglyceride levels in HDL, VLDL, CM or IDL.

For the reasons discussed above, the disclosure does not contain sufficient information regarding the subject matter of the claims as to enable one skilled in the art to make and use the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-17 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 is unclear as to what Applicants are determining in triglyceride. It is uncertain of the level, type, presence, and etc. contained in the lipoprotein.

Claim 5 is indefinite because the unit of measurement for molecular weight is missing.

Response to Argument

Any arguments from Applicants' remarks filed November 26, 2004 will be address as such.

6. Applicants argue that the disclosed methods are not limited to the determination of the triglyceride content of a single class of lipoproteins. Moreover, that the lipoprotein fraction can

be selectively adjusted. This argument has been fully considered, however, is not persuasive because Applicants have not provided any guidance to the parameters for determining the triglyceride level in HDL, VLDL, CM or IDL. Applicants state on page 4, lines 6-9, "Suitable influencing parameters here are the degree of polymerization or the polymerization length within the individual block units A or B and the arrangement and proportioning of the block units relative to the total copolymer" but do not describe the degree of polymerization length for the other lipoprotein fractions.

Applicants further argue that the composition of POP/POE block copolymer can be adjusted to selectively solubilize a particular lipoprotein class. This argument has been fully considered, however, is not persuasive because the specification does not describe what type of adjustment must be made for POP/POE block copolymer for determining the other lipoprotein class.

Applicants argue that one skill in the art could manipulate the block copolymer in order to selectively solubilize a specific lipoprotein. This argument has been fully considered, however, is not persuasive because the specification does not disclose how to manipulate the block copolymer for HDL, VLDL, CM or IDL. Applicants then argue that the selectivity to a particular lipoprotein class can be increased through agents for aggregation. The specification on page 5 only describes that the aggregation for LDL-associated triglyceride.

Conclusion

7. No claims are allowed.

Future Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to June Hwu whose telephone number is (571) 272-0977. The Examiner can normally be reached Monday through Thursday from 6:30 a.m. to 5:00 p.m.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JH

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